PATENT
Docket No. 760-248P

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICANTS: Shoji TSUJI et al.

APPLN. NO.: 09/101,132 GROUP: 1635

FILED: June 30, 1998 EXAMINER: J. Epps

FOR: cDNA FRAGMENT OF CAUSATIVE GENE OF SPINOCEREBELLAR ATAXIA TYPE 2

AMENDMENT

Assistant Commissioner of Patents
Washington, DC 20231

October 27, 1999

Sir:

In response to the Office Action dated April 27, 1999, the period for response having been extended three (3) months to October 27, 1999, the following amendments and remarks are respectfully submitted in connection with the above-identified application.

IN THE TITLE:

Please amend the title as follows:

cDNA FRAGMENTS OF <u>GENE</u> CAUSATIVE **[**GENE**]** OF SPINOCEREBELLAR ATAXIA TYPE 2

IN THE CLAIMS:

Please cancel claims 1-7.

Please add the following new claims:

--8. An isolated nucleic acid comprising a nucleotide sequence that encodes the amino acid sequence of SEQ. ID. NO.: 1 or the amino acid sequence of SEQ. ID. NO. :1 further comprising from 15 to 100 additional glutamine residues between amino acids 166 and 167.

9. The isolated nucleic acid of claim 8, comprising the nucleotide sequence of SEQ. ID. NO. 1 from residue 49 to 3987 or comprising the nucleotide sequence of SEQ. ID. NO. 1 from residue 49 to 3987 and further comprising from 15 to 100 repeats of the sequence CAA or CAG between nucleotides 546 and 547.

10. An isolated nucleic acid comprising a 2.5 kilobasepair Tsp E1 restriction fragment of human DNA that hybridizes to the nucleotide sequence of SEQ. ID. NO. 1 under conditions equivalent to 5 x SSC, 1 x Denhardt's solution, 10% sodium dodecyl sulfate, 20 mM sodium phosphate.

11. An isolated nucleic acid comprising a 630 basepair Sma I-Apa I restriction fragment of human DNA that hybridizes to the nucleotide sequence of SEQ. ID. NO. 1 under conditions equivalent to 5 x SSC, 1 x Denhardt's solution, 10% sodium dodecyl sulfate, 20 mM sodium phosphate.

12. An isolated nucleic acid comprising an antisense oligonucleotide of at least 15 basepairs that hybridizes to a mRNA comprising the nucleotide sequence of SEQ. ID. NO. 1, but wherein thymidine residues are replaced by uridine residues, so as to inhibit translation of said mRNA.

13. The isolated nucleic acid of claim 12, wherein said oligonucleotide is from 15 to 50 nucleotides in length.

14. A vector comprising an isolated nucleic acid according to any one of claims 8-13 operatively linked to a promoter effective for expressing said nucleic acid in a human cell.

15. A method for treatment of spinocerebellar ataxia comprising administering to a patient suffering from spinocerebellar ataxia the vector of claim 14 in an amount effective for providing a normal amount of SCA2 protein having from 15 to 25 glutamine residues between amino acids 150 and 172.

16. A method for genetic screening for spinocerebellar ataxia comprising:

i) contacting a sample comprising nucleic acid obtained from a subject with a first oligonucleotide of at least 15 nucleotides that

specifically hybridizes to the complement of SEQ. ID. NO.: 1 between positions 4367 and 622 and with a second oligonucleotide of at least 15 nucleotides that specifically hybridizes to the complement of SEQ. ID. NO.: 1 between nucleotides 1 and 543;

ii) performing a polymerase chain reaction using said sample nucleic acid as a template to obtain a product; and

iii) determining the length of said product;

wherein a finding of a length of said product indicating the presence of more than 35 triplets in the portion between nucleotides 544 and 622 indicates a predisposition to spinocerebellar ataxia.

17. The method of claim 16, wherein said first oligonucleotide comprises the nucleotide sequence of SEQ. ID. NO. 7 or SEQ. ID. NO. 8.

18. The method of claim 16, wherein said second oligonucleotide comprises the nucleotide sequence of SEQ. ID. NO. 6 or SEQ. ID. NO. 10.--

REMARKS

The Office Action of April 27, 1999, presents the examination of claims 1, 2 and 5-7, claims 3-4 having been withdrawn from consideration pursuant to restriction of the claims. Applicants

affirm the election of the claims of group I, claims 1, 2 and 5-7 for prosecution in this application. Applicants reserve the right to pursue the subject matter of the claims of the non-elected groups in application filed under 35 U.S.C. § 120.

Amendment to Title

The Official Filing Receipt indicated an error in the application's title as filed. However, Applicants accept the title as recorded on the Official Filing Receipt, and have amended the title herein in accordance therewith.

Priority Claim

Applicants attach hereto a certified English translation of the priority document.

Rejection Under 35 U.S.C. § 101

Claim 7 is rejected under 35 U.S.C. § 101 as encompassing a right in a human body. Claim 7 is canceled rendering the rejection moot.

Applicants submit that the Examiner has misunderstood the claim. The subject matter of claim 7, now presented in claim 15, is a method of treatment of spinocerebellar ataxia, not a claim to a transgenic human being. The method of claim 15, other than in the disease treated and the compound administered, is essentially the same as a claim to

treating a patient with a patented antibiotic compound. The owner of the patent covering penicillin does not obtain a property right in a patient taking the drug merely because that patient has taken it. If that were the case, then all methods for treatment of human beings would be non-statutory subject matter. This is clearly not so under present U.S. patent laws. Accordingly, the instant rejection should not be applied to the present claims.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claim 5 stands rejected under 35 U.S.C. § 112, first paragraph, for failure of the specification to provide description adequate to demonstrate that the Applicants had possession of the invention. Claim 5 is canceled, rendering this rejection moot. Applicants submit that the rejection should not be applied to the pending claims.

As the Examiner indicates, the purpose of the written description requirement is to establish that the Applicant had possession of the claimed invention as of the filing date of the application. Applicants submit that the present claims are fully described in the specification. The Examiner is referred, for example, to page 2, line 13; page 5, lines 5-10; page 10, line 3; page 14, lines 1-5 and lines 24-27; page 15, lines 7-27; page 16, lines 10-12; and Figure 1 (this shows a distinct instance of antisense oligonucleotides hybridizing to

an SCA2 gene). Applicants submit that the description of the invention provided above fully supports the present claims.

The Examiner also appears to include a "lack of enablement" ground in the rejection. Applicants submit that the present specification fully enables practice of the invention.

The Examiner indicates that the present target gene has many possible target sites for application of antisense inhibition of expression and that there is not sufficient information given to allow one of skill to determine which will be operable. The specification need not be a "production document". Details of the invention that are apparent to one of ordinary skill in the art, or that can be known from prior art, need not be included in the specification. Applicants submit that one of ordinary skill in the art, given the SCA2 sequence in the present specification, would understand what parts of the molecule are likely targets, e.g., the 5' UTR, and can apply knowledge in the art, for example computer programs that predict secondary structure, to refine a search for targets. Computer programs are also available that predict oligonucleotide sequences that would hybridize effectively to the mRNA.

The Examiner is further reminded that an expectation that screening for activity of an antisense oligonucleotide is expected in the art of molecular biology. Therefore, an experiment wherein several

oligonucleotides are synthesized and tested for activity should not be considered undue experimentation.

In support of Applicants' assertion, attached hereto is a Declaration under 37 CFR § 1.132 of Dr. Hisao Uchida. Dr. Uchida indicates his opinion, as one of ordinary skill in the art of antisense technology, that the present specification would be able to practice the antisense embodiments of the invention in view of the disclosure of the specification.

For all of the above reasons, Applicants submit that the present rejection of claim 5 should not be applied to the present claims.

Rejections Over Prior Art

Anticipation Rejection

Claims 1 and 2 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Pulst. This rejection is respectfully traversed as applied to the pending claims. Reconsideration and withdrawal thereof are requested.

Pulst is asserted as two references. The earlier is the direct GENBANK submission, Accession number U70323, sent to GENBANK on September 10, 1996. The second is a publication in *Nature Genetics* of November 14, 1996.

Applicants submit that the priority claim of the present application is sufficient to overcome the *Nature Genetics* reference.

As noted above, a verified English translation is attached hereto for consideration by the Examiner. As to the GENBANK submission, Applicants submit that the GENBANK submission is not a public disclosure. It is the policy of the GENBANK database to keep submissions confidential until publication of related journal articles. Applicants' Representative is in the process of confirming the actual release date of the data for Accession number U70323.

Obviousness Rejection

Claims 6 and 7 stand rejected under 103(a) as being unpatentable over Pulst et al. in view of Levinson. This rejection is respectfully traversed as applied to the pending claims. Reconsideration and withdrawal thereof are requested.

As explained above, the Pulst et al. reference, cited for the disclosure of the nucleotide sequence element of the rejected claims, is not prior art to the present application. Accordingly, the Examiner fails to make a *prima facie* case of obviousness of the invention from the cited references. Thus, the instant rejection should not be applied to the present claims.

If there are any minor matters precluding allowance of the application which may be resolved by a telephone discussion, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. (Reg. No. 36,623) at (703) 205-8000.

Pursuant to 37 C.F.R. § 1.17 and 1.136(a), Applicants respectfully petition a three (3) month extension of time for filing a response in connection with the present application. The required fee of $870.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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